

Office Action Summary

Application No.

10/567,544

Applicant(s)

GERRITS ET AL.

Examiner

KAGNEW H. GEBREYESUS

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 7-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 10/20/2008

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response on April 14, 2011 in response to the restriction requirement mailed on December 01, 2009 is acknowledged. The petition to revive this application was accepted on the grounds of unintentional delay. Applicants have elected the invention of group I comprising claims 1-6 without traverse. Claims 7-12 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups, there being no allowable or linking claims. Claims 1-6 are present for examination.

Priority

Acknowledgment of priority is made for this application filed on February 06, 2006 which is a national stage 371 application of PCT/EP2004/08469 filed on July 27, 2004.

Information Disclosure Statement

The information disclosure statement filed on October 20, 2008 for which a copy of the patent publication has been submitted in this application has been considered as shown by the Examiners signature.

Oath/Declaration

The oath or declaration submitted on October 20, 2008 has been reviewed and is in compliance with 37 CFR 1.56.

Drawings

The drawings are objected to because the hand written labels are unclear. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter. The disclosure is objected to because of the following informalities: At various portions of the specification, improper English is used. For example on page 3, lines 3-5 it is stated:

"Disturbing activities when producing lysates are eliminated only by that the content of the cell during the processing of the components important for the protein biosynthesis is fractioned."

This recitation is ambiguous. Applicants must revise the specification and provide a disclosure in proper idiomatic English for the most optimal examination of their application.

Furthermore the specification is objected to because the first line of the specification must contain cross-reference to related applications. In this case applicants do not state the benefit of filing from PCT/EP2004/08469 filed on July 27, 2004 for example.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Short et al. (Effects of Release Factor 1 on in Vitro Protein Translation and the Elaboration of Proteins Containing Unnatural Amino Acids *Biochemistry*, 1999, 38 (27), pp 8808-8819).

Claims 1-6 are drawn to a method for the production of a lysate used for cell-free protein biosynthesis wherein a gene encoding an essential endogenous translation factor such as release factor-1 (RF-1) is replaced by an exogenously/recombinant gene that encodes the same factor under a suitable regulatory element and a marker/tag sequence. Said recombinant organism is cultured, lysed and the marker/tag is used to separate the essential translation product thereby providing a lysate for the production of used for cell free biosynthesis of a desired protein.

Short et al teach an S-30 extract derived from *Escherichia coli* that expresses a temperature-sensitive variant of *E. coli* release factor 1 (RF1). Mild heat treatment of the S-30 extract partially deactivated RF1 and caused relaxed stringency of termination by RF1 at the stop codon (UAG) thus leading to improved UAG read through by as much as 11-fold. This was demonstrated by incorporation of unnatural amino acids into desired proteins (positions 25 and 125 of HIV-1 protease and positions 10 and 22 of *E. coli* dihydrofolate reductase). Furthermore increasing heat shock time the read-through increased.

Short et al do not teach that the RF-1 (an essential translation product) was removed from the lysate.

However Short et al teach that when RF1 was inactivated by heat shock the intrinsic rate of protein synthesis of HIV-1 protease or DHFR was increased.

Therefore it would have been obvious to one of ordinary skill in the art to remove the translation factor (RF1) from the lysate instead of using a temperature sensitive strain to achieve the same or better results. This is because applying heat to a lysate is likely to inactivate additional biomolecules necessary for protein synthesis. Furthermore it would have been obvious to include any on the tags mentioned in claim 3 which were available at the time of the instant

invention to and/or apply chromatographic method of separating the undesired factor available at the time of the instant invention to produce the lysate of the instant invention. One of ordinary skill in the art would have a reasonable expectation of success in producing increased amount of protein by removing the factor that competes at the stop codon with a suppressor tRNA that incorporates the unnatural amino acid.

Therefore based on Short's disclosure the inventions of claims 1-6 would have been *prima facie* obvious to a person of ordinary skill in the art of protein production and purification.

Conclusion: No claims are allowed.

Relevant reference:

1) Drugeon et al. Eukaryotic release factor 1 (eRF1) abolishes readthrough and competes with suppressor tRNAs at all three termination codons in messenger RNA.

Drugeon et al teach that the readthrough of termination codons located within the open reading frame (ORF) of mRNAs depends on the availability of suppressor tRNA(s) and the efficiency of eRF1 in translation termination *in cells*. They further state that an *in vitro* assay for release factor(s) (RF), activity based on the abolishment of readthrough by eRF1.

2) Stansfield I, Eurwilaichitr L, Akhmaloka, Tuite MF. Depletion in the levels of the release factor eRF1 causes a reduction in the efficiency of translation termination in yeast. *Mol Microbiol.* 1996 Jun;**20**(6):1135-1143

3) Bertram et al Microbiology (2001), 147, 225-269. Endless possibilities: translation termination and stop codon recognition. Bertram et al also teach that stop codon recognition by RF is in direct competition with suppressor tRNA (see page 263, 1st column).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MANJUNATH RAO can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KAGNEW H GEBREYESUS/
Primary Examiner, Art Unit 1656
August 11, 2011